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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SPIVACK, PHYLLIS G	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,112	TSUCHIMORI ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *6 and 8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 7, 9, 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1-12-05;12-13-07;2-11-08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicants' Response filed November 27, 2007 to the Restriction Requirement is acknowledged. Upon reconsideration the Restriction Requirement is withdrawn. The Response filed March 11, 2008 in response to a requirement for an Election of Species is further acknowledged. Applicants have elected the specie 1-acetyl -N-(3-{4-[4-(aminocarbonyl)benzyl)-1-piperidinyl}propyl)-N-(3-chloro-4-methylphenyl)-4-piperidinecarboxamide, which is also known as TAK 220.

Accordingly, the subject matter under initial consideration are those methods and agents for the treatment of graft-versus host disease and/or rejection reactions during organ or bone marrow transplantation comprising administering TAK 220. Claims 1-4, 9 and 10, are drawn to "An agent" and are considered composition claims. Claims 6 and 8 are presently withdrawn from consideration by the Examiner, as directed to non-elected inventions, 37 CFR 1.142(b).

Information Disclosure Statements filed January 12, 2005, December 13, 2007 and February 11, 2008 are acknowledged and have been reviewed.

The abstract of the disclosure is objected to because it is not drawn to the subject matter presently under consideration. Correction is required. See MPEP § 608.01(b).

Claim 7 provides for the use of a compound having a CCR antagonist effect, but since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 7 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 5 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for showing the preparation of various dosage forms and for the preparation of compounds having a CCR antagonist effect, does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. This is a Scope of Enablement rejection.

To be enabling, the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 27 USPQ 1510 (Fed. Circ.1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547,

the court recited eight factors to consider when assessing whether or not a disclosure would require undue experimentation. These factors are:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The invention is broadly drawn to the prevention and treatment of graft-versus host disease and/or rejection reactions during organ or bone marrow transplantation. As evidenced by The Merck Manual, the treatment for transplantation is still somewhat limited especially with respect to chronic rejection.

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. with expertise in the area of immunology.

However, that factor is outweighed by the unpredictable nature of attempting to maintain the functional integrity of the transplanted material in the recipient.

The instant specification provides support for preparing those compounds characterized as CCR antagonists and compositions comprising such compounds. The disclosure also provides background material directed to the general state of the art. The disclosure is clearly not predictable for prevention of any graft-versus host disease and/or rejection reactions during organ or bone marrow transplantation in a mammal. The skilled artisan would not reasonably expect that the claimed compounds could be used to prevent any occurrence – under any circumstance - of rejection reactions. A successful treatment modality for graft-versus host disease and/or rejection reactions does not presage success for preventing such conditions.

The breadth of the claims

The claims are very broad in that they are inclusive of any type of rejection reaction regardless of organ type.

The amount of direction or guidance provided and the presence or absence of working examples

There are no working examples drawn to treating or preventing any graft-versus host disease and/or rejection reaction during organ or bone marrow transplantation. No guidance is provided to distinguish types of organ or bone marrow problems to be prevented. Such an assertion is clearly beyond the scope of the instantly claimed

invention. The term "prevent" is an absolute definition that means to stop from occurring and thus requires a higher standard for enablement than does "therapeutic" or "treat". It is well established in the medical arts that the vast majority of diseases or conditions suffered by mankind cannot be totally prevented with current therapies.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to which particular compound would be preferred for preventing a particular type of graft-versus-host disease or organ rejection reactions that are encompassed in the language of instant claim 5. The skilled artisan would expect the interaction of a particular compound in the prevention of a particular type of rejection reaction to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for each agent. The instant specification sets forth no such understanding. Further, absent reasonable *a priori* expectations of success for using a "CCR antagonist" to treat a particular rejection reaction, one skilled in the immunology art would have to test extensively the many CCR antagonists that are known in the art to discover which particular type of rejection reaction responds to a particular compound and at the same time, prevents such pathology. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

Considering the state of the art, unpredictability of preventing graft-versus-host disease or organ rejection reactions and the total lack of support provided by the

specification for the claimed methods - support that is commensurate in scope with the claims - one of ordinary skill in the immunology arts would be burdened with undue experimentation to treat all forms of organ or bone marrow rejection reactions comprising administering the instantly claimed "CCR antagonists." Prevention entails the complete and absolute inhibition of the onset of any symptom of graft-versus-host disease and any manifestation thereof entirely.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-4, 9 and 10 are rejected under 35 U.S.C. 102(e), as being anticipated by Imamura et al., U.S. Patent 6,562,978.

Imamura teaches the compound 1-acetyl -N-(3-{4-[4-(aminocarbonyl)benzyl)-1-piperidinyl}propyl)-N-(3-chloro-4-methylphenyl)-4-piperidinecarboxamide, as in claim 2, column 232, and prepared as Example 376, column 202. Imamura teaches

compositions comprising the recited compounds in column 32, line 60, to column 33, line 22, as well as in column 230, lines 47-67, to column 231, line 15.

Intended use confers no patentable weight to composition claims. *See In* re *Hack*, 114 USPQ 161 (CCPA 1957). Merely reciting the intended use of an old composition does not impart patentability thereto.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The examiner can normally be reached on 10:30 AM-7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Ardin Marschel, can be reached on 591-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

May 21, 2008

/Phyllis G. Spivack/

Primary Examiner, Art Unit 1614